

# Exhibit 4

**In The Matter Of:**

*ARIOSA DIAGNOSTICS, INC.*

*v.*

*SEQUENOM, INC.*

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*EVANS, M.D., MARK I. - Vol. 1*

*April 27, 2012*

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***PURSUANT TO PROTECTIVE ORDER***

**MERRILL CORPORATION**

**LegaLink, Inc.**

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UNITED STATES DISTRICT COURT  
FOR THE NORTHERN DISTRICT OF CALIFORNIA  
--oo--

ARIOSA DIAGNOSTICS, INC.,  
(aka ARIA DIAGNOSTICS),

Plaintiff,

Case No.  
3:11-cv-06391-SI

v.

SEQUENOM, INC.,

Defendant/  
Counterclaim-Plaintiff.

v.

ARIOSA DIAGNOSTICS, INC.,  
(aka ARIA DIAGNOSTICS),

Counterclaim-Defendant,

and

ISIS INNOVATION LIMITED,

Nominal Counterclaim-  
Defendant.

/

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VIDEOTAPED DEPOSITION OF  
MARK I. EVANS, M.D.

Friday, April 27, 2012

Volume I (Pages 1 - 258)

REPORTED BY: CATHERINE RYAN, RMR, CRR, CSR 8239

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1	And what I was starting to say before we	12:20:35
2	got sidetracked a minute ago was that I remember	12:20:37
3	sitting at one of our three-times-a-year,	12:20:40
4	twice-a-year big group meetings shortly after the	12:20:45
5	paper came out and, you know, Dr. Bianchi,	12:20:48
6	Dr. Elias, Dr. Holzgreve and myself basically all	12:20:54
7	being what I would describe as shellshocked that	12:20:59
8	there was another and quite possibly much better way	12:21:01
9	of doing this than we had all spent a decade or more	12:21:03
10	working on, you know, within fetal cells, which	12:21:08
11	produced a lot of frustration.	12:21:11

12	Q And that's the discovery that fetal cells	12:21:13
13	exist in the plasma, right?	12:21:22

14	A No, we knew fetal cells existed in the	12:21:24
15	plasma in small numbers. The problem with fetal	12:21:28
16	cells was being able to use them accurately for	12:21:31
17	diagnosis.	12:21:33

18	Q How would a person of skill in the art	12:22:06
19	know in 1997 how you would, for example, amplify	12:22:12
20	paternally inherited nucleic acids from the serum or	12:22:20
21	plasma?	12:22:24

22	MR. HOLMES: Let me just interpose an	12:22:26
23	objection to the extent it calls for a legal	12:22:27
24	conclusion and vague.	12:22:29

25	BY MR. IANCU:	12:22:39
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1	Q	Do you have the question in mind, sir?
2	A	Yes. The technique of the polymerase
3		chain reaction was already well known in science at
4		that time as well as other methodologies which could
5		be used. So it was known that if one had paternally
6		derived nucleic acids of fetal origin, that one
7		could amplify them, at least in principle.
8	Q	And how would a person of skill in the art
9		know in 1997 how to detect the presence of a
10		paternally inherited nucleic acid of fetal origin in
11		the sample?
12		MR. HOLMES: Same objections.
13		THE WITNESS: I'm sorry. Could you repeat
14		the question, please?
15		BY MR. IANCU:
16	Q	How would a person of skill in the art in
17		1997 know how to actually detect the presence of
18		paternally inherited nucleic acid of fetal origin in
19		serum or plasma --
20		MR. HOLMES: Same objections.
21		BY MR. IANCU:
22	Q	-- of the mother?
23	A	Dr. Lo's paper published in the Lancet --
24		and I'd like to get it before I -- do we have a copy
25		of it here someplace? Okay. Dr. Lo's paper

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1	described methodology for -- for isolating maternal	12:24:19
2	plasma and then amplifying those sequences and then	12:24:37
3	detecting the presence of those acids.	12:24:42
4	Q Now, isolating maternal plasma is known	12:24:47
5	for a very long time, well before 1997, right?	12:24:51
6	A That one component is certainly known,	12:24:54
7	yes.	12:24:57
8	Q How do you do it, by the way?	12:24:57
9	A Basically, you can take a tube of blood	12:25:00
10	and just stick it on the table and it will clot off.	12:25:04
11	And then if you spin it, you get serum. If you	12:25:06
12	give anticoagulant so that the clotting factors	12:25:09
13	don't clump the cells, you get plasma. And then you	12:25:12
14	centrifuge it; so you separate out the cellular from	12:25:16
15	noncellular portions.	12:25:19
16	Q So taking the plasma, the maternal plasma,	12:25:25
17	if you know that you want to look in there for	12:25:28
18	paternally inherited nucleic acids of fetal origin,	12:25:30
19	how would one know what techniques to use? Was	12:25:34
20	there anything available how to do that, the actual	12:25:38
21	technology --	12:25:41
22	MR. HOLMES: Objection. Vague.	12:25:42
23	BY MR. IANCU:	12:25:43
24	Q -- in 1997?	12:25:44
25	A There are techniques that were being	12:25:52

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1	used to distinguish those cells in the maternal	12:28:20
2	circulation that came from the fetus as opposed to	12:28:25
3	that came from the mother.	12:28:28
4	BY MR. IANCU:	12:28:31
5	Q Once you know where you want to look for	12:28:31
6	the fetal cells, now that you want to look in the	12:28:35
7	plasma, for example, per Dr. Lo's 1997 paper, once	12:28:39
8	you know that --	12:28:44
9	A No, that's incorrect.	12:28:44
10	Q Apologies. Go ahead.	12:28:45
11	A Sorry.	12:28:47
12	MR. HOLMES: Dr. Evans, let --	12:28:47
13	THE WITNESS: I apologize.	12:28:49
14	MR. HOLMES: -- Mr. Iancu finish his	12:28:49
15	question.	12:28:53
16	THE WITNESS: Fair enough.	12:28:55
17	BY MR. IANCU:	12:28:55
18	Q I can often be incorrect; so I appreciate	12:28:56
19	you correcting me.	12:28:57
20	A Well, you said "fetal cells," not fetal	12:28:59
21	DNA.	12:29:01
22	Q Yes. Good. Thank you. I'm sorry.	12:29:01
23	Once you know where you want to look for	12:29:03
24	fetal DNA in the material -- in the maternal plasma,	12:29:05
25	as an example from -- per Dr. Lo's 1997 paper, the	12:29:10

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1	techniques for how to look for that DNA, how would	12:29:22
2	one of skill in the art know of those techniques at	12:29:35
3	that time?	12:29:36
4	MR. HOLMES: Objection. Vague.	12:29:37
5	THE WITNESS: Techniques such as the	12:29:39
6	polymerase chain reaction were known in the field at	12:29:40
7	that point.	12:29:43
8	BY MR. IANCU:	12:29:43
9	Q     And with that you can use to detect DNA,	12:29:44
10	correct?	12:29:47
11	A     Yes.	12:29:47
12	Q     Now, in your report at paragraph 47	12:29:50
13	through 50 you describe a variety of awards and	12:30:33
14	honors that you believe Dr. Lo received; is that	12:30:41
15	right?	12:30:44
16	A     That's correct.	12:30:45
17	Q     Go ahead and take a quick look through	12:30:46
18	that. I'll have a couple of questions on that.	12:30:50
19	A     Okay.	12:30:53
20	Q     My question, Dr. Evans, is: Specifically,	12:31:12
21	do you know what all of these awards were for in	12:31:21
22	paragraph 47, for example?	12:31:23
23	A     I do not know specifically what they were	12:31:43
24	for.	12:31:47
25	Q     Okay. So in paragraph 50 you indicated	12:31:49

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1	Q	Let me try, then -- let me ask a different	12:48:15
2		question. Who was it that made it known that	12:48:19
3		cell-free DNA was present in the maternal plasma in	12:48:20
4		detectable quantities?	12:48:24
5	A	Dr. Lo and Wainscoat.	12:48:26
6	Q	Anyone else?	12:48:32
7	A	Dr. Lo and Wainscoat had the sentinel	12:48:34
8		discovery, which resulted in the Lancet paper, other	12:48:38
9		papers and ultimately in the patents in question and	12:48:43
10		are regarded in the field as the pioneers who found	12:48:46
11		this and learned how to use it when no one else in	12:48:51
12		the field actively working on it thought it could	12:48:57
13		possibly be done.	12:48:59

14	Q	In the next sentence where you begin with	12:49:22
15		"Indeed," do you see that next sentence?	12:49:25
16	A	Okay.	12:49:27
17	Q	It ends with, quote, "Nobody thought that	12:49:28
18		fetal cell-free DNA would be present," closed quote;	12:49:31
19		do you see that?	12:49:39
20	A	Yes.	12:49:44
21	Q	Which you mean is that nobody thought that	12:49:45
22		fetal cell-free DNA would be present in the plasma?	12:49:46
23	A	In the maternal plasma.	12:49:50
24	Q	Right? Now, it was always there, right?	12:49:54
25	A	We now understand that it was there.	12:50:01

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1	A	Incredibly rare, but yes.
2	Q	Okay. Let's go to paragraph 104. Go
3		ahead and read that to yourself.
4	A	Okay.
5	Q	Others before Dr. Lo amplified and
6		detected nucleic acids, right?
7	A	Yes.
8	Q	In fact, traditional DNA diagnostics well
9		before 1997 traditionally involved three steps,
10		right: Sample preparation, amplification, and
11		detection, correct?
12		MR. HOLMES: Objection. Vague.
13		THE WITNESS: Commonly.
14	BY MR. IANCU:	
15	Q	And the others before Dr. Lo amplified and
16		detected nucleic acid in plasma or serum, true?
17	A	Yes.
18	Q	And, actually, amplifying and detecting
19		nucleic acids was done using fetal cells in maternal
20		blood for years before the '540 patent, right?
21	A	Repeat that again, please.
22	Q	Amplifying and detecting nucleic acids was
23		done using fetal cells in maternal blood for years
24		before the '540 patent, correct?
25		MR. HOLMES: I'm going to object to the

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1 the foregoing is true and correct. Subscribed at 05:22:51  
2 \_\_\_\_\_, California, this \_\_\_\_ day of 05:22:51  
3 \_\_\_\_\_, 2012. 05:22:51

4 05:22:51

5 05:22:51

6 \_\_\_\_\_ 05:22:51

7 MARK I. EVANS, M.D. 05:22:51

8 05:22:51

9 ---oo---

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**CERTIFICATE OF REPORTER**

2 I, **CATHERINE A. RYAN**, a Certified Shorthand  
3 Reporter, hereby certify that the witness in the  
4 foregoing deposition was by me first duly sworn to tell  
5 the truth, the whole truth and nothing but the truth in  
6 the within-entitled cause;

7           That said deposition was taken down in  
8 shorthand by me, a disinterested person, at the time and  
9 place therein stated, and that the testimony of the said  
10 witness was thereafter reduced to typewriting, by  
11 computer, under my direction and supervision;

12 That before completion of the deposition,  
13 review of the transcript [X] was [ ] was not requested.  
14 If requested, any changes made by the deponent (and  
15 provided to the reporter) during the period allowed are  
16 appended hereto.

17 I further certify that I am not of counsel or  
18 attorney for either or any of the parties to the said  
19 deposition, nor in any way interested in the event of  
20 this cause, and that I am not related to any of the  
21 parties thereto.

22 DATED: April 30, 2012

Catherine A Ryan  
(CATHERINE A. RYAN, CSR NO. 8239)